REMARKS

Claims.

The claims present in this divisional application are claims 32-46, with claims 37, 40, 42 and 43 withdrawn, and with claims 1-31 previously cancelled.

Rejection under 35 USC 103(a)

Claims 32-36, 38, 39, 41, 44-46

As unpatentable over US Patent 5,338,532 (Tomalia *et al.*)

Applicants contend that the present invention represents a selection invention over the cited Tomalia *et al.* '532 patent. The Examiner refers to the ability in the cited Tomalia *et al.* '532 patent to have a dendrimer conjugate transition metals such as YC_3 (*sic* YCl_3). YCl_3 is **not** a cancer agent so it would not be suitable for use the present method invention. Pt was not disclosed or taught in the cited Tomalia *et al.* '532 patent because of the need to administer Pt metal in a different organometallic form than Y, including issues for obtaining such a conjugate (page 9, lines 18-30) which is not the same process for the Y metal. The size differences in the resulting conjugates are also significant. The present Pt conjugate with cisplatin compounds may be as large as 44 nm in diameter, whereas Y is much smaller. The reactions conditions must be carefully controlled to make the present Pt conjugate too (rate of addition, time, temperature), none of which are described in the cited Tomalia *et al.* '532 patent. Thus no one skilled in the art would be able to make the present Pt conjugate without undue experimentation or having knowledge of this present process. Recently, Xinru Ji *et al.* from Peking University have found that these conjugates of a dendrimer and Pt do not form or exist in the expected manner. The negative charges on the surface provide sufficient repulsive force to counteract effects of the Van der Waals attraction and hydrogen bond interaction. If interparticle attraction doesn't occur, separated, size-monodisperse hard spheres would form an orderly array when particle concentration exceeds a critical volume fraction. [See also Frechet, J.M. and Tomalia, D.A., Dendrimers and Other Dendritic Polymers, 2001.]

The "platinum containing compounds" of the present invention must be useful as antineoplastic agents (page 10, lines 3-21). As Applicants explained in their prior response dated July 17, 2003, the present delivery system for cisplatin and its related compounds are for an organometallic Pt compound conjugated to a dendrimer and have never been made or commercially possible in the doses now available by this present method. These organic

metallic compounds do not behave for conjugation as the simple transition metal compound YCl_3.

These Pt compounds when conjugated to a dendrimer provide significant advantages over present known forms for administrating Pt. The currently, commercially available forms of cisplatin analogue sold under the name Paraplatin has warnings that its use requires adequate treatment facilities for its administration as of bone marrow suppression may occur which is the dose related, can be severe, anemia may be cumulative and require transfusion, and vomiting is frequent. Thus a better conjugate is clearly needed with fewer side effects which still can administer a higher dose of Pt for treatment of the patient. The present invention meets that need.

The present conjugate had to be made to test its stability, retaining activity when delivered *in vivo*, lowering toxicity from the known forms of injected cisplatin, and the amount of loading of active possible into the conjugate. These factors could not be predicted from the cited Tomalia *et al.* '532 patent. Also an "obvious to try" is not an acceptable standard for rejection. There is no way to predict whether such combination of elements would work for the intended purpose. Please review and reconsider our remarks in this regard in our response dated July 17, 2003, page 7, last paragraph through page 8, end of the last full paragraph.

This invention concerns a method for use of a drug-delivery system. The active agent must remain effective *in vivo* at the desired site of delivery (which is the usual required for all drug delivery systems). Thus the dendrimer portion, whether it releases that active drug or not, must not interfere with the effectiveness of the drug at the desired site. In this invention not only does this delivery system succeed at that objective, but its stability is increased while retaining activity when delivered *in vivo*, and its toxicity and significant side effects to the patient are reduced from the known forms of injected cisplatin, and it can be administered in larger doses for effectiveness by increasing the amount of loading of active drug possible into the conjugate. These results attained by this present method would not have been predicted by one skilled in cisplatin administration or by knowledge of the cited Tomalia et al.'532 patent.

CONCLUSION

Applicants believe that all rejections presented in the Office Action mailed October 22, 2003 have been overcome by this Response. Applicants respectfully request that the

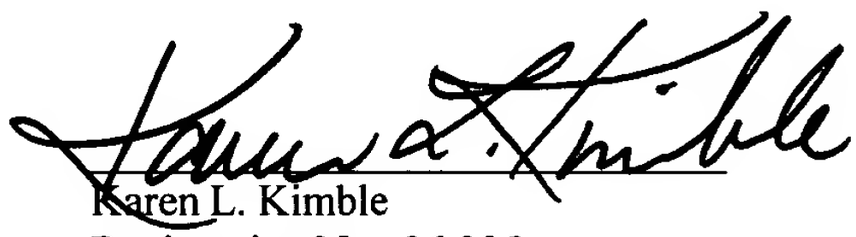
rejections be reconsidered in light of these remarks and that all pending claims 32-36, 38, 39, 41 and 44-46 and withdrawn claims 37, 40, 42 and 43 be allowed.

Applicants request that if (a) there are issues remaining unresolved regarding any points raised by this Action or (b) no claims are found allowable after consideration of this Response but that some possible claim amendment may render all or some claims allowable, then an interview be granted at a mutually convenient time either by telephone or in person.

NOTICE OF APPEAL

The appropriate Notice of Appeal is provided to permit Applicants to supply an appeal brief, if needed, after the Examiner's consideration of this Response.

Respectfully submitted,



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